UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/345,148	06/30/1999	ANDREW H. SEGAL	3378/80490	9870

29933 7590 07/02/2003

PALMER & DODGE, LLP
KATHLEEN M. WILLIAMS
111 HUNTINGTON AVENUE
BOSTON, MA 02199

EXAMINER	
GAMBEL, PHILLIP	

ART UNIT	PAPER NUMBER
1644	20

DATE MAILED: 07/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	09/345,148	SEGAL
	Examiner	Art Unit
	GAMBEL	1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☑ Responsive to communication(s) filed on 4/00/03

2a)☑ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☑ Claim(s) _____ is/are pending in the application. 1, 3-17, 19-68, 70

4a) Of the above claim(s) _____ is/are withdrawn from consideration. 15-16, 19, 20, 27, 30-68

5)☐ Claim(s) _____ is/are allowed.

6)☑ Claim(s) _____ is/are rejected. 1, 3-14, 17, 21-25, 28, 29, 70

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☑ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☐ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4)☐ Interview Summary (PTO-413) Paper No(s). _____.
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other:

DETAILED ACTION

1. Applicant's amendment, filed 4/10/03 (Paper No. 17), has been entered.
Claims 2, 18 and 69 have been canceled.
Claims 17, 23, 28, 29 and 70 have been amended.

Claims 1, 3-17, 19-68 and 70 are pending.

For the record, applicant's election of the species CD40-specific antibody, alpha chain of C3b and IL-2 in Paper No. 10, filed 4/5/01 and in Paper No. 13, filed 12/19/01, has been acknowledged.

Claims 1, 3-14, 17, 21-25, 28, 29 and 70 are being acted upon as the elected invention

Claims 15-16, 19, 20, 27 and 30-68 have been withdrawn from consideration by the examiner 37 CFR 1.142(b), as being drawn to a nonelected inventions and/or species.

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Action.
This Office Action will be in response to applicant's arguments, filed 4/10/03 (Paper No. 17).
The rejections of record can be found in the previous Office Action (Paper No. 15).

3. The substitute specification in compliance with applicant's statements filed, 4/10/03 (Paper No.19), has been entered and is in compliance with 37 CFR 1.125(b).

4. Upon reconsideration of applicant's comments, filed 4/10/03 (Paper No. 17), the previous rejection under 35 U.S.C. § 112, second paragraph.

5. Claims 1, 5-9 and 15 stand rejected under 35 U.S.C. § 102(e) as being anticipated by Maraskovsky et al. (U.S. Patent No. 6,017,527) (see entire document) essentially for the reasons of record set forth in the last Office Action (Paper No. 20).

Applicant's arguments, filed 4/10/03 (Paper No. 17), have been fully considered but are not found convincing essentially for the reasons of record.

Applicant submits that the present claims relate to methods of vaccinating a mammal to a selected antigen comprising administering a vaccine comprising a CD40 ligand-enhanced cell, wherein the CD40 ligand of the CD40 ligand-enhanced cell is engineered (that is, comprises a heterologous cell membrane binding moiety).

Applicant asserts that the present specification defines an engineered CD40 ligand as a ligand for CD40 that comprises a heterologous cell membrane binding moiety (page 10, lines 30-32) (actually page 11, lines 7-8 of the original specification and page 11, lines 10-11 of the substitute specification).

Applicant asserts that "engineered" in the context of the present invention does not merely mean that the CD40 ligand is produced recombinantly, but instead requires that the CD40 ligand include a heterologous cell membrane binding moiety.

However, the patentability of a product does not depend on its method of production. In re Thorpe, 227 USPQ 964, 966 (Fed. Cir. 1985). See MPEP 2113.

It appears that all that is required of the claims is "the administration of a vaccine composition comprising a CD40 ligand-enhanced cell", that is, a CD40 ligand-enhanced cell capable of modulating an immune response to a selected antigen (see page 9, paragraph 1 of the substitute specification).

The claims do not require the administration of "an engineered ligand for CD40", that is "a ligand for CD40 that comprises a heterologous cell membrane binding moiety" (see page 11, lines 7-8 of the original specification and page 11, lines 10-11 of the substitute specification) as a separate step in the instant claims.

Here, the "CD40 ligand-enhanced cell" is met by the prior art teaching of antigen-expressing activated dendritic cells and, in turn, the instant claims are met by the prior art teaching of vaccination with antigen-expressing activated dendritic cells, including stimulating immune responses with the administration of other cytokines such as the CD40 ligand and IL-2 (e.g. see column 6, paragraph 1; column 11, paragraph 4).

It is presumed that equivalent products can be obtained by multiple routes. The burden is on the applicant to establish a patentable distinction between the claimed and referenced antigens and the methods to make said products.

Further, it is noted that page 13, paragraph 1 of the substitute specification discloses that "it is preferred that the cell membrane binding moiety bind to a cell by a means other than interaction of a polypeptide with its cognate cell-surface polypeptide".

However, the claims do not necessarily limit the claims to the preferred disclosed embodiments.

The claims can broadly encompass various molecules or polypeptides that bind a cell, resulting in a "CD40 ligand enhanced cell"..

Maraskovsky et al. teach the methods of vaccination with antigen-expressing activated dendritic cells, including stimulating immune responses with the administration of other cytokines such as the CD40 ligand and IL-2 (e.g. see column 6, paragraph 1; column 11, paragraph 4). Here, transfecting the dendritic cells to express the cytokines is also taught. The patentability of a product does not depend on its method of production. In re Thorpe, 227 USPQ 964, 966 (Fed. Cir. 1985). See MPEP 2113.

Maraskovsky et al. teach antigens from a number of pathogenic organisms encompassed by the claimed invention, including bacteria, virus tumor associated antigens (see Preparation of Antigens on columns 10-11).

Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the referenced methods to vaccinate with antigen-expressing activated dendritic cells with CD40 ligand and/or IL-2 separately or co-transfected to various pathogenic organisms.

Applicant's arguments are not found persuasive.

6. Claims 1 and 5-9 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Maraskovsky et al. (U.S. Patent No. 6,017,527) in view of (Dullforce et al. (Nature Medicine 4: 88-91, 1998; 1449) AND/OR Heath et al. (Eur. J. Immunol., 24: 1828-1834, 1994) AND/OR and Caux et al. (Research in Immunology 145: 235-239, 1994) essentially for the reasons set forth in the previous Office Action (Paper No. 15).

Applicant's arguments, filed 4/10/03 (Paper No. 17), have been fully considered but are not found convincing essentially for the reasons of record.

Applicant essentially argues that the cited combination of prior art does not teach all of the claimed limitations.

Applicant asserts that Maraskovsky does not teach an engineered CD40 lignad which comprises a heterologous cell membrane binding moiety.

Applicant argues that the secondary references do not remedy the teachings of the primary reference.

The examiner's rebuttal concerning the breadth of the claims and the lack of requiring a separate step with respect to "engineered CD40 ligand" is addressed above.

In contrast to applicant's assertions, the following of record is reiterated for applicant's convenience.

Maraskovsky et al. teach the methods of vaccination with antigen-expressing activated dendritic cells, including stimulating immune responses with the administration of other cytokines such as the CD40 ligand and IL-2 (see entire document, including column 6, paragraph 1; column 11, paragraph 4). Here, transfecting the dendritic cells to express the cytokines is also taught.

Maraskovsky et al. teach antigens from a number of pathogenic organisms encompassed by the claimed invention, including bacteria, virus tumor associated antigens (see Preparation of Antigens on columns 10-11).

It is noted that Maraskovsky et al. teach that anti-CD40 antibodies have been shown to mediate various biological activities (see column 7, lines 61-65). However, Maraskovsky et al. differs from the claimed methods by not disclosing the administration of agonistic CD40-specific antibodies per se.

Dullforce et al. teach the administration of agonistic CD40-specific antibodies as adjuvants to stimulate B cells and antigen presenting cells against bacterial pathogens (see entire document, including Abstract). While Dullforce et al. focus on T cell-independent immune responses, it would have been obvious to one of ordinary skill in the art at the time the invention was made that the administration of known agonistic anti-CD40 antibodies would have been applicable to various pathogenic organisms and antigens. It is noted that anti-CD40 antibodies stimulate antigen presenting cells and that human B cells are antigen presenting cells.

Heath et al. teach anti-CD40 antibodies, including various epitopic specificities, that are capable of stimulating immune responses such as B cells as well as the use of such antibodies in infectious diseases and malignancy (page 1833, column 2) (see entire document, including Abstract and Discussion).

Caux et al. teach the expression of functional CD40 on B lymphocytes and dendritic cells (see entire document).

Given the teachings of Maraskovsky et al. of employing stimulation immune responses via the CD40 pathway, it would have been obvious to one of ordinary skill in the art to employ the known agonistic anti-CD40 antibodies, taught by Heath et al. and Caux et al., in the methods of vaccinating with antigen-expressing activated dendritic cells, taught by Maraskovsky et al.

One of ordinary skill in the art at the time the invention was made would have been motivated to select agonistic CD40 antibodies to stimulate immune responses via CD40 expressing antigen presenting cells to increase the immune response to antigen expressing dendritic cells to a variety of pathogenic organisms. As pointed out above, Maraskovsky et al. teach combining antigen expressing activated dendritic cells with other reagents that costimulate immune responses (see column 11, paragraph 4). In addition to the teachings of agonistic CD40-specific antibodies, taught by Dullforce et al., heath et al. And Caux et al., it was well known and practiced at the time the invention was made to generate recombinant antibodies such as chimeric antibodies, humanized antibodies and fragments thereof to decrease immunogenicity and increase half-life of such recombinant antibodies. Therefore, the engineered CD40-specific antibodies encompassed the claimed invention would have been obvious to one of ordinary skill in the art at the time the invention was made. The patentability of a product does not depend on its method of production. In re Thorpe, 227 USPQ 964, 966 (Fed. Cir. 1985). See MPEP 2113. Such anti-CD40 antibodies would comprise the idiotypic portion of an antibody which binds CD40.

From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments are not found persuasive.

7. Claims 1, 5-14, 17, 21-25, 28 and 29 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Maraskovsky et al. (U.S. Patent No. 6,017,527) in view of Dullforce et al. (Nature Medicine 4: 88-91, 1998; 1449) AND/OR Heath et al. (Eur. J. Immunol., 24: 1828-1834, 1994) AND/OR and Caux et al. (Research in Immunology 145: 235-239, 1994).
as applied to claims 1, 2, 5-9 and 15 above and further in view of the well known use of engineering attachment of a lipid such as a long-chain fatty acid to a molecule such as a peptide to permit the complex to stably associated with the plasma membrane , including the use of palmitate as acknowledged on pages 64- 67 of the instant specification (see Engineered Opsonins, Cytokines or Ligands for CD40 Containing a Lipid), including the teachings of McHugh et al. (PNAS 92: 8059-8063, 1995) essentially for the reasons of record set forth in the last Office Action (Paper No. 15).

Applicant's arguments, filed 4/10/03 (Paper No. 17), have been fully considered but are not found convincing essentially for the reasons of record.

Applicant essentially argues that the cited combination of prior art does not teach all of the claimed limitations.

Applicant asserts that Maraskovsky does not teach an engineered CD40 ligand which comprises a heterologous cell membrane binding moiety.

Applicant argues that the secondary references do not remedy the teachings of the primary reference.

The examiner's rebuttal concerning the breadth of the claims and the lack of requiring a separate step with respect to "engineered CD40 ligand" is addressed above.

In addition, applicant submits that McHugh teaches a construct comprising a GPI moiety linked to CD40 ligand or the use of such an engineered CD40 ligand in a mixture with an antigen bearing cell for the purpose of vaccinating a mammal, but McHugh acknowledges that the specific teachings relating to GPI-B7 are unpredictable (see page 8063, paragraph 1).

Applicant asserts that Maraskovsky teaches away from using an engineered CD40 ligand, comprising a heterologous cell membrane binding moiety

A prior art reference may be considered to teach away when "a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant." In re Gurley , 27 F.3d 551, 553, 31 USPQ2d 1130, 1131 (Fed. Cir. 1994). General skepticism of those in the art -- not amounting to teaching away -- is also "relevant and persuasive evidence" of nonobviousness. Gillette Co. v. S.C. Johnson & Son, Inc. , 919 F.2d 720, 726, 16 USPQ2d 1923, 1929 (Fed. Cir. 1990). In effect, "teaching away" is a more pointed and probative form of skepticism expressed in the prior art.

In contrast to applicant's assertions that the McHugh reference stands for "unpredictability" and provides no motivation for coupling the GPI to other desired proteins, the following is noted.

McHugh teaches that the GPI-B7 molecule was demonstrated to be easily incorporated into many different cell lines (see entire document, including the Discussion, page 8063, column 1, paragraph 1). Further, McHugh note that other costimulatory molecules have been demonstrated (page 8063, column 1, 3). Here, the reference concludes by stating that molecules can be quickly tested, individually or in cooperation with others, to determine the proper combination need to create immunogenic cells that may be used in therapy (page 8063, column 1, 3).

In response to applicant's arguments that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See In re Fine 5 USPQ2d 1596 (Fed. Cir 1988) and In re Jones 21 USPQ2d 1941 (Fed. Cir. 1992).

The following of record is provided for applicant's convenience.

In this case the combined teachings provide for enhancing / activating antigen presenting cells via CD40 to generate immune responses to solve or address the same or similar problems or endpoints encompassed by the claimed invention by one of ordinary skill in the art at the time the invention was made. The strongest rationale for combining reference is a recognition, expressly or implicitly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent that some advantage or expected beneficial result would have been produced by their combination In re Sernaker 17 USPQ 1, 5-6 (Fed. Cir. 1983) see MPEP 2144

The teachings of Maraskovsky et al. in view of Dullforce et al. AND/OR Heath et al. AND/OR and Caux et al. have been set forth above and differ from the claimed methods as they read on methods of employing lipid linked anti-CD40 antibodies, encompassed by the breadth of the claims.

Pages 64- 67 of the instant specification (see Engineered Opsonins, Cytokines or Ligands for CD40 Containing a Lipid) provide for a number of teachings that acknowledge the well known use of engineering attachment of a lipid such as a long-chain fatty acid to a molecule such as a peptide to permit the complex to stably associated with the plasma membrane , including the use of palmitate.

Given that co-stimulatory nature of the CD40:CD40 ligand pathway and the co-stimulatory signal provided by anti-CD40 antibodies, the teachings of McHugh et al. are particularly relevant to the instant invention.

In exemplifying potent immune responses to tumor cells, McHugh et al. teach the use introducing costimulatory molecules into membranes via glycosyl-phosphatidylinositol (GPI) as an alternative approach to provide costimulatory molecules to stimulate immune responses of interests (see entire document, including page 8059, column 2, paragraphs 2-3, Materials and Methods, Results and Discussion). McHugh et al. teach that this eliminates the introduction of foreign DNA for tumor immunotherapy, for example, (see Introduction and Discussion). McHugh et al. teach combinations of costimulatory signals to create the optimal target to facilitate many T cell regulatory and effector functions (see page 8063, column 1, paragraph 3).

Again, McHugh et al. focus on tumor immunity, but one of ordinary skill in the art would have been motivated to employ GPI anchored co-stimulatory molecules with immunogenic cells to stimulate immune responses of interest.

Given the teachings and advantages of combining co-stimulatory molecules via alternative methods as taught by the above-mentioned references, one of ordinary skill in the art at the time the invention was made would have been motivated to modify antigen presenting dendritic cells with GPI anchored agonistic antibodies to increase stimulation to pathogenic organisms.

Alternative methods of producing a lipid-linked engineered anti-CD40 antibodies or cytokines by chemically linked the polypeptide to a fatty acid such as palmitate is also acknowledged by the instant specification (see Engineered Opsonins, Cytokines or Ligands for CD40 Containing a Lipid, particularly page 67, paragraph 2).

Further, given the teachings of Maraskovsky et al. of vaccinating for tumor antigens, including the use of CD40:CD40 ligand pathway and IL-2 (see above) and the teachings of McHugh et al. for teaching the provision of co-stimulatory signals in conjunction with tumor cell vaccination, the ordinary artisan would have been motivated at the time the invention was made to combine the co-stimulatory signal of anti-CD40 antibodies, taught by Dullforce et al., Caux and Heath, in conjunction with the tumor cells themselves to vaccinate against tumor cells and/or antigens of interest. It would have been immediately apparent to one of ordinary skill in the art that tumor cells would have been attenuated so that tumor cells would not be able to divide and proliferate in a host. If not, the tumor cells could proliferate to the point of being detrimental to the subject for the vaccination.

Therefore, one of ordinary skill in the art would have been motivated to select agonistic CD40 antibodies to stimulate immune responses via CD40 expressing antigen presenting cells and/or tumor cells via GPI, as taught by McHugh et al., to increase the immune response to antigen expressing dendritic cells and/or tumor cells to a variety of pathogenic organisms, including tumor antigens as well as the those antigens encompassed by the bacteria, fungi and parasites. As pointed out above, Maraskovsky et al. teach combining antigen expressing activated dendritic cells with other reagents that costimulate immune responses (see column 11, paragraph 4).

In addition to the teachings of agonistic CD40-specific antibodies, taught by Dullforce et al., Heath et al. and Caux et al., it was well known and practiced at the time the invention was made to generate recombinant antibodies such as chimeric antibodies, humanized antibodies and fragments thereof to decrease immunogenicity and increase half-life of such recombinant antibodies. Such anti-CD40 antibodies would comprise the idiotypic portion of an antibody which binds CD40. Given the well known use and practice of recombinant technology to produce homogeneous proteins at the time the invention was made, engineered CD40-specific antibodies as well as engineered cytokines encompassed by the claimed invention would have been obvious to one of ordinary skill in the art at the time the invention was made. The patentability of a product does not depend on its method of production. In re Thorpe, 227 USPQ 964, 966 (Fed. Cir. 1985). See MPEP 2113.

From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments are not found persuasive.

8. Claims 3, 4 and 70 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Maraskovsky et al. (U.S. Patent No. 6,017,527) in view of Dullforce et al. (Nature Medicine 4: 88-91, 1998; 1449) AND/OR Heath et al. (Eur. J. Immunol., 24: 1828-1834, 1994) AND/OR and Caux et al. (Research in Immunology 145: 235-239, 1994).
as applied to claims 1, 5-14, 17, 21-25, 28, and 29 above and further in view of
and in further view of the known use of engineering attachment of a lipid such as a long-chain fatty acid to a molecule such as a peptide to permit the complex to stably associated with the plasma membrane , including the use of palmitate as acknowledged on pages 64- 67 of the instant specification (see Engineered Opsonins, Cytokines or Ligands for CD40 Containing a Lipid).McHugh et al. (PNAS 92: 8059-8063, 1995)
and further in view of Jacquier-Sarlin et al. (Immunology 84: 164-170, 1995)
essentially for the reasons of record set forth in the previous Office Action (Paper No. 15).

Applicant's arguments, filed 4/10/03 (Paper No. 17), have been fully considered but are not found convincing essentially for the reasons of record.

Applicant essentially argues that the cited combination of prior art does not teach all of the claimed limitations.

Applicant asserts that Maraskovsky does not teach an engineered CD40 lignad which comprises a heterologous cell membrane binding moiety.

Applicant argues that the secondary references do not remedy the teachings of the primary reference and that there was insufficient motivation to combine the references.

The examiner's rebuttal concerning the breadth of the claims and the lack of requiring a separate step with respect to "engineered CD40 ligand" is addressed above.

The following of record is reiterated for applicant's convenience.

Maraskovsky et al. in view of Dullforce et al. AND/OR Heath et al. AND/OR and Caux et al. further in Engineered Opsonins, Cytokines or Ligands for CD40 Containing a Lipid on pages 64-67 of the instant specification, including the teachings of McHugh et al differs from the claimed invention by not teaching the addition of the alpha chain of C3b.

Jacquier-Sarlin et al. teach the use of complement fragments including C3b to enhance immune responses to antigens of interest (see entire document). By increasing antigen processing and presentation, C3b could be engineered into new vaccines (see Discussion, particularly the last paragraph on page 169).

Given the teachings of Jacquier-Sarlin et al. that C3b which would include the alpha chain of C3b, increases antigen processing and presentation which would be useful for engineering vaccines, one of ordinary skill in the art would have been motivated to incorporate C3b into vaccine preparations to a host of pathogenic organisms and antigens, including tumor antigens in order to increase immunogenicity and, in turn, increase immune responses to antigens of interest.

Therefore, it would have obvious to a person of ordinary skill in the art at the time the invention was made to apply the teachings of Jacquier-Sarlin to incorporate C3b into the methods of vaccination via alternative modes of compositions comprising immunogenic cells, anti-CD40 antibodies and IL-2, as taught above to obtain vaccination by a highly immunogenic composition to pathogenic organisms of interest, including tumor cells. The motivation to combine can arise from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combine for their common known purpose, which is increasing immunogenicity in methods of vaccination in the instant case. From the teachings of the references; it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments are not found persuasive.

9. No claim is allowed.

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

PHILLIP GAMBEL

Phillip Gambel, PhD.
Primary Examiner
Technology Center 1600
June 23, 2003